Effect of Reconstruction Parameters in High-Definition PET/CT on Assessment of Lymph Node Metastases in Head and Neck Squamous Cell Carcinoma

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Phantom studies showed that images reconstructed with 3-mm gaussian postfiltering gained a higher image quality and signal-to-noise ratio. Best results for true-positive lymph node findings were achieved with 3-mm postfiltering. With 1-mm postfiltering, accuracy lesion detection was not improved, because increasing sensitivity (95% true-positive) correlated with decreasing specificity (12% false-positive). Conclusion: For lymph node assessment on a high-resolution PET/CT scanner, we consider the OSEM algorithm with 3 iterations and 24 subsets, combined with 3-dimensional 3-mm gaussian postfiltering, to be optimal. The continuous application of presently established PET protocols in patients with HNSCC will prove whether current acquisition and reconstruction methods are valuable and should be maintained.

Key Words: head and neck squamous cell carcinoma; lymph node metastasis; 18F-FDG PET/CT; FWHM; gaussian filter

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Despite current imaging concepts that include CT, MR tomography, and PET/CT, diagnosis of early-stage head and neck squamous cell carcinoma (HNSCC) and involved lymph node metastases remains a challenge (1–3). Considering that this tumor entity represents the fifth most common cancer worldwide, with HNSCC being newly diagnosed in 500,000 people every year, only accurate preoperative staging can improve primary tumor response and locoregional control (4,5). Therapeutic outcome and overall survival in patients with HNSCC very much depends on local primary tumor size, infiltration of adjacent vascular structures, and presence and spread of lymph node metastases at the time of diagnosis (6). 18F-FDG PET/CT meanwhile is an established imaging modality for lymph node staging in HNSCC, achieving high overall diagnostic sensitivity, specificity, and accuracy of more than 90% (1,3,7,8).

Hybrid PET/CT delivers combined anatomic and functional information. It is part of the oncologic work-up of tumors with regard to diagnosing, staging, and evaluating therapy response (9). Especially in the head and neck region, with its small anatomic structures, special attention is
required for optimal diagnostic throughput. In this setting, the selection of dedicated scanning protocols and image reconstruction parameters plays an important role (10). Iterative reconstruction techniques in combination with application of various spatial gaussian postfilters influence spatial resolution of PET images, image contrast, and signal-to-noise ratio (SNR) (10,11).

The purpose of this study in patients with an initial diagnosis of HNSCC was the optimization of reconstruction parameters in high-definition (HD) PET/CT for improved diagnostic assessment of lymph node metastases. We also investigated the influence of parameter settings on image quality and on standardized uptake value (SUV) monitoring of suggestive cervical lymph nodes in HNSCC.

MATERIALS AND METHODS

Phantom Study

The imaging quality study was performed using a body phantom from the National Electrical Manufacturers Association (NEMA)/International Electrotechnical Commission with 6 fillable spheres, with a radius from 10 to 37 mm to simulate hot and cold lesions. A cylindric insert filled with low-atomic-number material (0.3 ± 0.1 g/mL) was used to simulate attenuation. The background activity concentration was 5 kBq/mL, with a hot-to-background ratio of 4:1, similar to those found in the head and neck region. To simulate the activity out of the scanner, a line source approximately 70 cm long with an activity of 109 MBq was inserted in a large solid polyethylene cylinder. The data were acquired in list mode for 3 min per bed scan. The images were reconstructed using an ordered-subset expectation maximization (OSEM) algorithm with 3 iterations and 24 subsets. The following reconstruction parameters were used: a matrix size of 200 × 200 (pixel size, 4.07 mm); zoom of 1; and gaussian filters of 1, 3, and 6 mm in full width at half maximum (FWHM). This procedure was performed 3 times in order to check the reproducibility of the results. Reconstructed images were analyzed with the image quality test following the NEMA protocol NU2-2007 (12). The purpose of the image quality test was to evaluate the image contrast (\( Q \)). The percentage contrast for hot lesions (10, 13, 17, and 22 mm) and cold lesions (28 and 37 mm) are defined in Equations 1 and 2, respectively. \( C \) is the average count of any region and \( a \) is the activity concentration, with the subindices \( H \) for hot and \( B \) for background for spheres of size \( f \).

\[
Q_{H,j} = \frac{C_{H,j}/a_H - 1}{a_H/a_B - 1} \times 100\% \tag{1}
\]

\[
Q_{C,j} = \left(1 - \frac{C_{C,j}}{C_{B,j}}\right) \times 100\% \tag{2}
\]

SNRs were calculated for 7 plastic cylinders (diameters varying from 4.4 to 22.0 mm with volumes of 0.5–20.0 mL) that were placed in an adaptation to the Ultra Delux Jaszczyk Phantom manufactured in house in order to fit within a circular distribution with the larger cylinder in the center. The smaller cylinder size was closer to the spatial resolution reported by the manufacturer (4.5 mm). Because the injected amount of \( ^{18} \text{F}-\text{FDG} \) also depends on patient weight, activities of 350 and 200 MBq were analyzed. Initially, the spheres were filled with \( ^{18} \text{F} \), with an activity concentration of 5 kBq/mL. After 83 min, a second activity of 2.86 kBq/mL was applied.

The SNR was defined according to Equation 3 as the ratio of the mean value of a region of interest (ROI) of 2 × 2 pixels (mean-ROI\(_{a,b} \)) minus the mean background ROI of 20 × 20 pixels (mean\(_B \)) over the SD in the background (SD\(_B \)). The SNR was calculated for gaussian filters of 1, 3, and 6 mm in FWHM and also for reconstructed images without any postprocessing filter method.

\[
\text{SNR} = \frac{\text{mean-ROI}_{a,b} - \text{mean}_B}{\text{SD}_B} \tag{3}
\]

For each reconstructed series, the factors of Equation 3 were calculated, with an ROI drawn in the center of each cylinder for a total of 3 slides.

Patients

Between September 2009 and June 2011, 54 patients (14 women and 40 men; mean age, 59 y; age range, 36–84 y), with an initial diagnosis of HNSCC were referred to our Institute of Clinical Radiology and Nuclear Medicine for staging with \( ^{18} \text{F}-\text{FDG} \) PET/CT. Before the PET/CT examination, all patients had been seen clinically by an experienced ear, nose, and throat surgeon. The prospective study was approved by our hospital institutional ethic review committee. All patients who enrolled gave written informed consent for undergoing staging PET/CT before therapy. After PET/CT all patients underwent neck dissection. For anatomic correlation between imaging findings and surgery, the neck dissection specimen were divided into individual cervical lymph node levels (13). The histologic work-up of the lymph nodes served as the gold standard.

The diagnosis of HNSCC was confirmed histologically in all patients. The primary tumor locations were the base of the tongue (\( n = 16 \)), tonsil (\( n = 10 \)), oropharynx (\( n = 7 \)), larynx (\( n = 8 \)), hypopharynx (\( n = 4 \)), and oral cavity (\( n = 4 \)). Five patients presented with cancer of unknown primary where the tumor could not be located despite neck dissection in cervical lymph node metastases that were present.

PET/CT and Image Interpretation

Patients were imaged according to a dedicated head and neck protocol on a Biograph mCT HD PET/CT scanner with a high-counting-rate lutetium oxyorthosilicate detector (Siemens Healthcare Sector). After a fasting period of at least 6 h, a weight-adapted intravenous injection of 250–300 MBq of \( ^{18} \text{F}-\text{FDG} \) (ZAG Zyklotron AG) was administered. Approximately 60 min after tracer application, 780-mm CT using attenuation correction and a low-dose extended field of view was performed (slice thickness, 5 mm; increment, 3 mm). The anterior–posterior CT topogram was used for planning and determining the bed positions. The acquisition time for 1 bed position was 3 min. Emission images were acquired in 3-dimensional mode. After PET, high-resolution contrast-enhanced biphasic CT from the skull base to the chest was performed on every patient (tube voltage, 120 kV; tube current, 50–120 mAs; slice collimation, 16 × 1.2 mm; pitch, 0.8; rotation time, 0.5 s).

All studies were reconstructed into a 200 × 200 matrix (zoom, 1) using a resolution-recovery 3-dimensional OSEM algorithm (3 iterative steps, 24 subsets). The postfiltering used in this study was a 3-dimensional gaussian filter. To study the effect of smoothing filter strength on diagnostic accuracy in the head and neck area,
we used 1, 3, and 6 mm in FWHM as cutoffs to perform reconstructions. The head and neck, a region with low attenuation levels, requires less image postfiltering and preferably more than 2 iterations to achieve good image quality with reduced noise \((10)\).

To minimize partial-volume effect and optimize spatial resolution specifically, 1, 3, and 6 mm in FWHM were chosen. The average reconstruction processing time for a whole-body study was 13 min. Suggestive lymph nodes and their maximum SUV were documented on an evaluation sheet individually for the right and left sides of the neck and according to an established neck lymph node level classification \((13)\). For determination of \(^{18}\)F-FDG uptake in suggestive lymph nodes, regions of interest were individually drawn around the lesions and calculated. Maximum SUV was measured and documented on the readers’ sheet. Considering manufacturer-dependant hardware and software equipment for the PET/CT scanner, a maximum SUV threshold of 3.5 or less was associated with a benign lymph node not infiltrated by tumor, whereas a maximum SUV threshold of 3.5 or more was characteristic of a lymph node metastasis.

The image quality of the lymph nodes, randomly displayed in 1, 3, and 6 mm in FWHM, was evaluated visually. Two experienced independent readers performed a visual and semiquantitative analysis of the cervical lymph nodes to determine whether they were benign or malignant. Neither observer was aware of the reconstruction parameters used or the histologic findings of the lymph nodes. In the readings, all suggestive lymph nodes, including lymph nodes in the head and neck region that appeared nonmalignant, were considered. Reading was based entirely on the PET information without corresponding CT images having been viewed. Differences in reading were solved by consensus. Lymph nodes that were suggestive on PET and histologically confirmed as malignant were classified as true-negative findings. Lymph nodes that were not suggestive on PET but were histologically confirmed as benign were classified as false-positive findings. Lymph nodes that were suggestive on PET but were histologically confirmed as malignant were classified as false-negative findings. Sensitivity, specificity, and statistical significance of lymph node detection and accurate diagnostic assessment at 1, 3, and 6 mm in FWHM were evaluated and compared, using a paired \(t\) test.

**RESULTS**

For the phantom studies, the visual differences in image quality on the transaxial sections of the reconstructed images for different FWHM filters are displayed in Figure 1. The most apparent observation was that postfiltering at 1 mm in FWHM produced images of high noise, compared with the smooth images obtained at 6 mm. The edges of the hot and cold lesions changed with filter size and were rounder with 6-mm postfiltering than with 1 mm. The summary of the results for image quality are presented in Table 1. The image contrast \((Q)\) was the only parameter that changed between the selected filters and was higher for 1-mm than for 3- or 6-mm postfiltering. Nevertheless, the differences between 1 and 3 mm were not mathematically significant for either hot and cold regions or small and big lesions. For 6 mm, compared with 1 mm, the difference was around 10% less for any lesion.

The results for SNR for different lesion sizes are summarized in Table 2 for each activity. The increase of the SNR was proportional to filter and region size and the applied doses. For small lesions (4.4 mm), the ratio between 6 and 1 mm in FWHM was 1.3 and 2.0 times for each activity ratio, respectively. The proportion was lower between 3 and 1 mm in FWHM (1.3 for 200 MBq and 1.2 for 350 MBq). This proportion was also applicable to the larger studied region of 19.9 mm. Nevertheless, the omission of postfiltering showed a better SNR than the use of 1-mm postfiltering for any region. This effect could not be demonstrated with 3-mm postfiltering.

In the 54 patients, 123 lymph nodes were evaluated on PET and histologically correlated with the neck dissection specimen. Histopathology of the dissection specimens showed 41 benign lymph nodes and 82 malignant lymph nodes (Fig. 2). The images postfiltered at 3 and 1 mm, despite more noise, demonstrated the lymph node findings with more contrast than did the much smoother images.

**TABLE 1**

Phantom Study for Image Quality with 1, 3, and 6 mm in FWHM

<table>
<thead>
<tr>
<th>Sphere size (mm)</th>
<th>Gaussian filter (mm in FWHM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>32.0 ± 4.4</td>
</tr>
<tr>
<td>13</td>
<td>56.8 ± 2.6</td>
</tr>
<tr>
<td>17</td>
<td>63.0 ± 4.0</td>
</tr>
<tr>
<td>22</td>
<td>75.0 ± 4.9</td>
</tr>
<tr>
<td>28</td>
<td>64.7 ± 1.6</td>
</tr>
<tr>
<td>37</td>
<td>66.8 ± 1.4</td>
</tr>
</tbody>
</table>

Data are image contrast \((Q)\) (%).
postfiltered at 6 mm. The impact of partial-volume effect was less in 1- and 3-mm postfiltered images than in 6-mm images. For lymph node assessment, CT information was not available for the readers. The overall image quality of the reconstructed postfiltered PET images improved from 6 mm in FWHM to 3 mm in FWHM, with significantly better lymph node visibility and contour detection despite increased noise (Fig. 3). Especially in small lymph nodes, metastatic involvement could be diagnosed more accurately on 1- and 3-mm postfiltered images, whereas in enlarged necrotic lymph node metastases no obvious difference in image quality among 1-, 3-, and 6-mm postfiltered images could be noted (Fig. 3).

Depending on the gaussian filter applied for image reconstruction, significant differences ($t$ test $P < 0.0001$) in maximum SUV levels between benign and malignant lymph nodes could be demonstrated (Table 3). With decreasing size of the gaussian filter, the accuracy of lymph node characterization and SUV measurement increased, although no significant difference between 3- and 1-mm postfiltering was visible (Table 3). There was no overlap of the confidence intervals. They underlined the accurate distinction of maximum SUV levels in benign and malignant lymph nodes in each filter group: 6 mm in FWHM: benign lymph nodes, 2.7–3.1, and malignant lymph nodes, 3.7–4.6; 3 mm in FWHM: benign lymph nodes, 3.0–3.5, and malignant lymph nodes, 4.2–5.3; and 1 mm in FWHM: benign lymph nodes, 2.9–3.5, and malignant lymph nodes, 4.3–5.4.

Both readers were equally experienced in the sensitivity analysis of consensus reading. The overall sensitivities for correctly diagnosed lymph nodes were best in 3-mm postfiltered images (Table 4). With 1 mm in FWHM, no increase of accurate lesion detection was observed, because increasing sensitivity (95% true-positive lymph node findings) correlated with decreasing specificity (12% false-positive lymph node findings).

The gaussian filter–based receiver-operating-characteristic analysis of the maximum SUV levels for benign and malignant lymph nodes demonstrated statistically significant results in all 3 groups (Table 5). Postfiltering with 1 mm in FWHM showed the best area under the curve results and the most accurate delineation between benign and malignant lymph nodes (Table 5). Most probably because of the small number of patients, no significant differences were observed between the groups with 1- and 3-mm postfiltering.

**DISCUSSION**

$^{18}$F-FDG PET/CT is a well-accepted diagnostic tool for lymph node staging in HNSCC, and its impact on assessment of residual or recurrent lymph node metastases in the
of neck patient with cancer of unknown primary (CUP; thick straight arrow) did not differ in any postfiltered images despite increased image blurring with 6 mm in FWHM.

neck after surgery and radiochemotherapy is equally high (14,15). The more precise the initial staging performed, the better the expected posttherapeutic outcome for the patient. Over the last decade, technical issues in PET/CT have continuously been addressed, resulting in improved scanner technology with sensitive lesion detection and advanced data processing (8,15,16). Imaging of the head and neck, an anatomically small region compared with studies of the whole body, requires dedicated imaging protocols and reconstruction algorithms to achieve sensitive and specific lesion detection (17).

In this observer study with 2 experienced readers, an OSEM algorithm was applied on a Biograph mCT scanner for PET image reconstruction in patients with an initial diagnosis of HNSCC. The intention was to analyze the effect of varying gaussian-filter strengths on image quality and sensitivity of lymph node metastasis detection. Considering that the spatial resolution of the Biograph mCT (18) is around 4.5 mm for the specific image reconstruction used in this study and the average size of the lymph nodes was around 10–15 mm, we adapted standard postfiltering with 1, 3, and 6 mm in FWHM. In all patients, diagnostic findings could be correlated with histopathology after neck dissection.

Previously, Gutman et al. (19) have reported about the influence of iterations, subsets, and filter strengths on the diagnostic image quality of PET. Postfiltering of PET images for noise reduction has also been described but without consideration of a new scanner technology, such as established with the Biograph mCT (20–22). In our phantom study, the use of postprocessing filter methods with 1 mm in FWHM did not bring about an improvement in image quality. The only benefit was the increase of contrast, but the SNR was similar to images being obtained without any filter. A significant change could be noticed with the 3 mm in FWHM. A high contrast could be achieved, similar to that obtained with 1 mm in FWHM and higher than that obtained with 6 mm in FWHM. Also, the SNR was improved for any ROI. The application of a thicker FWHM resulted in improved SNR but reduced contrast. This effect could be confirmed during the patient study, in which 1 mm in FWHM did not contribute significantly to diagnostic information on PET images. These results are consistent with the publication by Akamatsu

<table>
<thead>
<tr>
<th>Gaussian filter (mm)</th>
<th>Histology</th>
<th>Lymph nodes</th>
<th>Mean maximum SUV</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Benign</td>
<td>41</td>
<td>2.89</td>
<td>0.59</td>
<td>2.2</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td>Malignant</td>
<td>82</td>
<td>4.20</td>
<td>1.94</td>
<td>1.8</td>
<td>11.0</td>
</tr>
<tr>
<td>3</td>
<td>Benign</td>
<td>41</td>
<td>3.23</td>
<td>0.73</td>
<td>2.4</td>
<td>6.4</td>
</tr>
<tr>
<td></td>
<td>Malignant</td>
<td>82</td>
<td>4.77</td>
<td>2.39</td>
<td>1.4</td>
<td>13.6</td>
</tr>
<tr>
<td>1</td>
<td>Benign</td>
<td>41</td>
<td>3.25</td>
<td>0.81</td>
<td>1.7</td>
<td>6.8</td>
</tr>
<tr>
<td></td>
<td>Malignant</td>
<td>82</td>
<td>4.85</td>
<td>2.43</td>
<td>2.5</td>
<td>14.6</td>
</tr>
</tbody>
</table>
In the clinical study, the best scores for lesion detection were achieved with 1 and 3 mm postfiltering. For each filter used, maximum SUV per lesion could be evaluated accurately, allowing distinction between potentially benign and malignant lymph nodes without overlap of the confidence intervals. Postfiltering with 3 mm in FWHM delivered the highest sensitivity and specificity scores for detection of lymph node metastases. The 1-mm postfiltering resulted in increased sensitivity but decreased specificity for lesion detection and therefore cannot be recommended by us for standard PET image reconstruction in the head and neck region.

Besides physical parameters that can affect PET acquisition and reconstruction, the SUV too, which is influenced by tracer kinetics, can affect image quality and interpretation (20,22). Yet, physiologic parameters such as movement by the patient, inflammation, and blood glucose levels can raise maximum SUV levels and make distinction between benign and malignant lymph nodes difficult, despite advanced image postprocessing software. Therefore, despite the good diagnostic quality of PET images after postfiltering with 3 mm in FWHM, we cannot establish a general recommendation for image reconstruction in PET.

Komar et al. analyzed 2-dimensional and 3-dimensional 18F-FDG PET with different acquisition times (24). Acquisition time influenced uptake parameters in the patients in both modes, but surprisingly, maximum SUV levels did not differ between the 2-dimensional and 3-dimensional PET modes. In our study with fixed iterations and subsets, a significant filter-dependent difference in maximum SUV cutoff levels for benign and malignant lymph nodes was observed (Table 3). Six millimeters in FWHM clearly led to an underestimation of SUV measurements for benign and malignant lymph nodes. Three and 1 mm in FWHM contributed to sensitive and specific lesion detection. These findings were in line with the experience of Gutman et al. (19) and Boellard (22). PET postfiltering with a change of spatial resolution affects SUV quantification and diagnostic outcome. Postfiltering with 1 mm in FWHM could not increase diagnostic output significantly, because increased sensitivity for lesion detection correlated with decreased specificity. One of the probable reasons for specificity reduction due to the small postprocessing filter is related to the partial-volume effect. This effect, produced by the combination of resolution, reconstruction process, and image sampling, influences lesions of less than twice the resolution, that is, lesions of approximately 11 mm (25,26). In these cases, the application of correction factors as recovery coefficients is a solution, especially in oncologic imaging, but this issue was beyond the scope of the present study.

One of the limitations of this study was the fact that only PET information was available for the readers at the time of investigation. Therefore, the role of lymph node size and its correlation with the SUV with regard to benign or malignant lesion remained unconsidered in this study.

The manufacturer-dependant hardware and software of each PET scanner has to be taken into consideration. With

<table>
<thead>
<tr>
<th>Gaussian filter (mm)</th>
<th>Histology</th>
<th>No. of lymph nodes</th>
<th>True-positive finding</th>
<th>False-positive finding</th>
<th>True-negative finding</th>
<th>False-negative finding</th>
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<tbody>
<tr>
<td>6</td>
<td>Malignant</td>
<td>95</td>
<td>73</td>
<td>22</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Benign</td>
<td>28</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Malignant</td>
<td>112</td>
<td>79</td>
<td>33</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Benign</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1</td>
<td>Malignant</td>
<td>114</td>
<td>78</td>
<td>36</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Benign</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
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</table>

No. of total lymph nodes: 82, malignant; 41, benign.

<table>
<thead>
<tr>
<th>Gaussian filter (mm)</th>
<th>Histology</th>
<th>Mean maximum SUV</th>
<th>Total area under curve, k-values</th>
<th>$P &gt; \chi^2$</th>
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</thead>
<tbody>
<tr>
<td>6</td>
<td>Benign</td>
<td>2.89</td>
<td>0.76</td>
<td>$&lt; 0.0001$</td>
</tr>
<tr>
<td></td>
<td>Malignant</td>
<td>4.2</td>
<td>0.76</td>
<td>$&lt; 0.0001$</td>
</tr>
<tr>
<td>3</td>
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<td>3.23</td>
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<td>$&lt; 0.0001$</td>
</tr>
</tbody>
</table>
the integration of time-of-flight imaging in PET, a reduction of examination time and improvement of image quality due to decreased blurring can be expected (27). The characteristics of time-of-flight projections, being organized in time bins along each line of response with improved estimation of the actual image, are presently being evaluated by us in patients with HNSCC.

**CONCLUSION**

Compared with previous imaging protocols, for lymph node assessment on a high-resolution PET/CT scanner we consider the OSEM algorithm with 3 iterations and 24 subsets, combined with a 3-dimensional gaussian postfiltering with 3 mm in FWHM, optimal for lymph node staging. The continuous application of presently established PET protocols in patients with HNSCC will prove whether current acquisition and reconstruction methods are valuable and should be maintained.

**DISCLOSURE**

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**REFERENCES**


